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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/773,861	02/01/2001	Gregory M. Landes	GA0182US	5135

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EXAMINER	
SOUAYA, JEHANNE E	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 05/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/773,861	LANDES, GREGORY M.	
	Examiner	Art Unit	
	Jehanne E Souaya	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-32* is/are pending in the application.

4a) Of the above claim(s) *4-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The examiner reviewing your application at the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to examiner Jehanne Souaya.

1. Currently, claims 1 and 3 are under consideration in the instant application. Claim 2 has been canceled. Claims 4-32 are withdrawn from consideration as being drawn to non elected inventions. Claims 1 and 3 have been amended. The rejections with regard to claims 1-3 in the previous office action are moot in view of the amendments to the claims and the cancellation of claim 2. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. The following rejections are newly applied, necessitated by amendment. This action is FINAL.

2. With regard to the recitation of "corresponds to" in claim 1, while the previous office action rejected the claim under 35 USC 112/2nd paragraph and indicated such term indefinite, the rejection is withdrawn in view of the amendment to claim 1 which makes clear the definition of the term "corresponds to" in step a of claim 1. In step a, it is clear that the recitation of "corresponds to" means that the polynucleotide encodes the polypeptide. Therefore, although this term is still present in the claim, the rejection is withdrawn in view of the amendments to the claim and definition of the term in step a) of the claim.

New Grounds of Rejection

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Natzle et al (The Journal of Biological Chemistry, vol. 261, pp 5575-5583; 1986).

The claim is drawn to a method of identifying a polynucleotide which encodes a secreted or membrane bound polypeptide comprising obtaining a polynucleotide from a microsomal fraction, wherein the microsomal fraction is obtained from a cellular homogenate by centrifugation, and identifying the sequence of the polynucleotide and it's expression level. Natzle et al specifically teach a method whereby a gene encoding a pupal cuticle protein, known to be secreted by Drosophila imaginal discs, was obtained by a microsomal fraction of a cellular homogenate. Natzle specifically teaches that an initial preparative centrifugation step concentrated microsomal material and thus allows efficient sucrose flotation gradient banding of the membrane bound polysomes (see p. 5576, col. 1, 2nd full para in "Results" section). Natzle then teaches that the membrane associated RNA was prepared by phenol extraction. Natzle teaches that mRNA obtained from this fraction was analyzed and a pupal cuticle protein known to be secreted by imaginal disks was identified. Therefore, the sequence of the polynucleotide

taught by Natzle was identified. By determining that the polynucleotide was expressed, Natzle teaches "determining its expression level". It is noted that the recitation of "identifying the sequence of the polynucleotide and its expression level" was not interpreted to be limited to sequencing the polynucleotide or determining its expression level relative to a certain level. The claim does not specifically recite either embodiment, and has not been interpreted to be limited to such. Therefore, Natzle et al anticipate the limitations of the claimed invention.

5. Claims 1 and 3 are rejected under 35 U.S.C. 102(e) as being anticipated by Einat et al (US Pre Grant Publication 2002/0037511; 102(e) date: 5/11/1998).

Claim 1 is drawn to a method of identifying a polynucleotide which encodes a secreted or membrane bound polypeptide comprising obtaining a polynucleotide from a microsomal fraction, wherein the microsomal fraction is obtained from a cellular homogenate by centrifugation, and identifying the sequence of the polynucleotide and it's expression level. Claim 3 specifies that the identifying step comprises serial analysis of gene expression (SAGE).

Einat et al teach a method that "synergistically integrates" two types of previously known methodologies, wherein the first method is the division of cellular mRNA into separate pools of mRNA derived from different cellular fractions, and the second method is the simultaneous analysis of the relative abundance of the mRNA species found in the separate pools (see p. 3, section 0034). Einat et al teach specifically: a method for identifying genes whose expression is responsive to a specific cue or cues including the steps of a) applying a cue to an organism or tissue or cells, b) isolating specific cellular fractions, such as cytoplasmic, nuclear, polyribosomal, microsomal, mitochondrial, and/or splicesome (see claim 7 of Einat), from the

tissues or cells subjected to the cue, c) extracting the mRNA from the cellular fractions, and d) differentially analyzing the mRNA samples in comparison with control samples to identify genes that have responded to the cue (see claim 1 of Einat et al). Einat et al specifically teach using SAGE for the differential analysis step, (see claim 8 of Einat et al), teach to identify and measure the genes regulated at the translation or transcription level (claims 9 and 10 of Einat et al), and teach that the genes identified include genes encoding secreted or membrane bound proteins (claim 14 of Einat et al) which Einat et al specifically teach are obtained from the microsomal fraction (table 1). Einat et al also specifically teach that isolating specific cellular fractions, including the fraction containing microsomes, is achieved using centrifugation of cellular homogenate (see figure 1A, and pp 6-7, sections 0078-0082). While the instant claims do not specifically recite step a of Einat et al (applying a cue to an organism or tissue or cells), the instantly claimed invention is drawn to a method which "comprises" steps, which encompasses prior art methods that teach each limitation of the claimed method steps as well as additional steps. Therefore, because the method of Einat et al teach every limitation of the claimed invention, the method of Einat et al anticipates the claimed invention.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Natzle et al in view of Kinzler et al (WO 97/10363).

Claim 3 is drawn to a method of identifying a polynucleotide which encodes a secreted or membrane bound polypeptide comprising obtaining a polynucleotide from a microsomal fraction, wherein the microsomal fraction is obtained from a cellular homogenate by centrifugation, and identifying the sequence of the polynucleotide and it's expression level using serial analysis gene expression (SAGE).

Natzle et al teach a method of isolating and characterizing nucleic acids encoding membrane bound and secreted proteins by isolating the mRNA from the microsomal fraction of cellular homogenate. Natzle et al teach that a preparative centrifugation step concentrates microsomal material and thus allows efficient sucrose flotation gradient banding of the membrane bound polysomes (that contain transcripts encoding membrane bound and secreted proteins). Natzle et al teach that RNA from this fraction was prepared using phenol extraction (see p. 5576-col. 1). Natzle et al teach that a number of different transcripts were isolated from this fraction, including a protein known to be secreted (see col. 2, first line, table 1). Natzle teaches that analysis of the transcripts from both the microsomal fraction and the cellular fraction was carried out using a number of different methods, which included probing with P^{32} labeled nick translated cDNA on RNA transcripts immobilized on nitrocellulose filters (see p. 5576, col. 2, lines 6-8), in vitro translation of membrane associated and cytoplasmic fractions (col. 2, first full para), and differential hybridization screening to determine the identify of transcripts encoding membrane associated proteins whose expression is hormone dependent (p. 5576, end of col. 2, -5579). Natzle et al do not teach analyzing the transcripts isolated from the microsomal

fraction using SAGE, however Kinzler et al teach that SAGE is an improved method that allows for the rapid analysis of numerous transcripts in order to identify the overall pattern of gene expression in different cell types or in the same cell type under different physiologic or pathologic conditions (see p. 4, para 1). Kinzler et al teach that the method involves the use of a short nucleotide sequence tag, which is used to identify the corresponding transcript and gene from which it is transcribed. Kinzler et al teach that a sequence tag for a sample can be compared to corresponding information in a sequence database to identify known sequences that match the sample sequence, thereby identifying the sequence of the transcript (see p. 18). Kinzler et al specifically teach examples wherein SAGE was used to characterize gene expression in human pancreas (see p. 22) and to specifically identify transcripts (see p. 27) and novel expressed genes (see p. 28-29). Kinzler et al teach that such method is an improvement over prior art techniques such as cDNA subtraction, differential display, EST tags, Northern blotting, RNase protection, and RT PCR analysis. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the method of isolation and analysis of transcripts encoding membrane bound or secreted proteins of Natzle et al, by substituting the improved analysis method of Kinzler et al with the analysis method of Natzle et al to arrive at the instantly claimed invention because Kinzler et al teach that SAGE is an improved method of analyzing the identity and level of expression of mRNA transcripts from a sample with numerous transcripts. The ordinary artisan would have recognized that such method of analysis would be applicable to the pool of unknown and uncharacterized transcripts obtained by the isolation method taught by Natzle et al. The ordinary artisan would have been motivated to improve the method of the Natzle et al, that is isolation and

analysis of nucleic acid transcripts encoding membrane bound and secreted proteins, with the SAGE method taught by Kinzler et al for the purpose of making the method of Natzle et al easier to perform.

Conclusion

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. No claims are allowable over the cited prior art.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703) 308-6565. The examiner can normally be reached Monday-Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Souaya

Jehanne Souaya
Patent examiner
Art Unit 1634
5/8/03